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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,861	02/07/2002	Kevin M. Slawin	675.002US1	1421
21186	7590	04/05/2006	EXAMINER	
SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH 121 S. 8TH STREET SUITE 1600 MINNEAPOLIS, MN 55402			NEGIN, RUSSELL SCOTT	
		ART UNIT	PAPER NUMBER	
		1631		

DATE MAILED: 04/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	10/071,861	SLAWIN ET AL.
	Examiner	Art Unit
	Russell S. Negin	1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 05 January 2006.
- 2a) This action is FINAL.                            2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 28-42 is/are pending in the application.
- 4a) Of the above claim(s) 1-27 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 28-42 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
	6) <input type="checkbox"/> Other: _____.

## **DETAILED ACTION**

### ***Specification***

The objection to the abstract is withdrawn due to modifications made by the applicant to the abstract in the response of January 5, 2006.

### ***Claim Rejections - 35 USC § 112***

The rejections of claims 28-36 under 35 U.S.C. 112, first paragraph, are withdrawn due to both amendments made to the claims and arguments in the specification on pages 10-12 in the reply of January 5, 2006.

The rejections of claims 28, 29, 32, 34, 35, and 36 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn due to amendments made by the applicant to the set of claims in the reply of January 5, 2006.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 28, 29, 32, 34, and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Ivanovic [Nature Medicine, Volume 1, 1995, pages 282-283].

Claims 28, 29, 32, 34 and 35 are apparatuses and methods for determining the prognoses of prostate cancer patients comprising: a data input means, for input of test information comprising the level or amount of at least one protein in a physiological fluid sample obtained from a human, wherein the at least one protein is selected from the group consisting of various species of protein including transforming growth factors; and a processor, executing the software for analysis of the level or amount of the at least one protein in the sample; wherein the software analyzes the level or amount of the at least one protein in a physiological sample from a human prostate cancer patient treated for clinically localized prostate cancer and provides the risk of prostate cancer progression in the patient.

Claim 32 examines prostate specific antigen as well.

In Ivanovic, the second paragraph states, "TGF-beta1 and prostate specific antigen (PSA) were analyzed from the same plasma samples and the data presented vertically coincident for each patient (see figure). Plasma from BPH patients [benign prostatic hyperplasia] contained  $2.47 \pm 0.64 \text{ ng ml}^{-1}$  TGF-beta1 (see table), a value similar to the  $3.99 \pm 0.77 \text{ ng ml}^{-1}$  observed for non-BPH males, and published normal values. These results indicate that unlike PSA, plasma TGF-beta1 is not elevated in BPH patients."

The third paragraph continues, "Twelve 'primary' CaP patients (patients for whom TGF-beta1 values were obtained while all or most of their prostate was intact) were incorporated into the study, six with pathological stage II (with tumour confined to the prostate), and six with pathological stage III/IV disease (with tumour having extensive

extracapsular extension, seminal vesicle invasion, lymph node metastases or distant metastases)."

The apparatus and processors used are described on page 283, column 1, lines 4-11, of Ivanovic which state, "The TGF-beta1 and PSA values for each patient coincide on the vertical scale. TGF-beta1 was measured directly from plasma by the PREDICTA TGF-beta1 kit (Genzyme Diagnostics, Cambridge, Massachusetts, USA) specific for activated form of TGF-beta1. However, the detected plasma TGF-beta1 is in latent form, as immunoreactivity in both controls and CaP samples was totally abolished when plasma samples were not acid treated (unpublished data). The absorbance at 450 nm and extrapolation of unknown TGF-beta1 concentrations from the standard curves were performed on an EL Microplate ELISA reader (BIO-TEK Instruments, Highland Park, Vermont, USA)."

This computer system, software and processors generate the data shown in the Table of page 282 of Ivanovic, which tabulates the concentrations of TGF-beta1 and PSA measured from these instruments to determine the prognosis of prostate cancer.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28-31, 32, 34, 35, and 37-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ivanovic [Nature Medicine, volume 1, 1995, pages 282=283].

Claims 28-31, 32, 34, 35, and 37-42 state:

Claims 28, 29, 34 and 35 are apparatuses and methods for determining the prognoses of prostate cancer patients comprising: a data input means, for input of test information comprising the level or amount of at least one protein in a physiological fluid sample obtained from a human, wherein the at least one protein is selected from the group consisting of various species of protein including transforming growth factors; and a processor, executing the software for analysis of the level or amount of the at least one protein in the sample; wherein the software analyzes the level or amount of the at least one protein in a physiological sample from a human prostate cancer patient treated for clinically localized prostate cancer and provides the risk of prostate cancer progression in the patient.

Claim 32 examines prostate specific antigen as well.

Claims 37-42 dictate when the test is completed (i.e. before or after therapy for prostate cancer).

In Ivanovic, the second paragraph states, "TGF-beta1 and prostate specific antigen (PSA) were analyzed from the same plasma samples and the data presented vertically coincident for each patient (see figure). Plasma from BPH patients [benign prostatic hyperplasia] contained  $2.47 \pm 0.64 \text{ ng ml}^{-1}$  TGF-beta1 (see table), a value similar to the  $3.99 \pm 0.77 \text{ ng ml}^{-1}$  observed for non-BPH males, and published normal values. These results indicate that unlike PSA, plasma TGF-beta1 is not elevated in BPH patients."

The third paragraph continues, "Twelve 'primary' CaP patients (patients for whom TGF-beta1 values were obtained while all or most of their prostate was intact) were incorporated into the study, six with pathological stage II (with tumour confined to the prostate), and six with pathological stage III/IV disease (with tumour having extensive extracapsular extension, seminal vesicle invasion, lymph node metastases or distant metastases)."

The apparatus and processors used are described on page 283, column 1, lines 4-11, of Ivanovic which state, "The TGF-beta1 and PSA values for each patient coincide on the vertical scale. TGF-beta1 was measured directly from plasma by the PREDICTA TGF-beta1 kit (Genzyme Diagnostics, Cambridge, Massachusetts, USA) specific for activated form of TGF-beta1. However, the detected plasma TGF-beta1 is in latent form, as immunoreactivity in both controls and CaP samples was totally abolished when plasma samples were not acid treated (unpublished data). The absorbance at 450 nm

and extrapolation of unknown TGF-beta1 concentrations from the standard curves were performed on an EL Microplate ELISA reader (BIO-TEK Instruments, Highland Park, Vermont, USA)."

This computer system, software and processors generate the data shown in the Table of page 282 of Ivanovic; which tabulates the concentrations of TGF-beta1 and PSA measured from these instruments to detect the prognosis of prostate cancer.

Ivanovic does not show whether these tests are administered before or after therapy of prostate cancer.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice Ivanovic both before and after therapy of the prostate cancer, because the therapy does not affect the integrity, or procedure of the test itself; the chronology of the test is irrelevant in determining the prognosis of the disease.

Claims 28, 29, 33 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ivanovic as applied to claims 28-31, 32, 34, 35, and 37-42 above, and further in view of Kattan [Journal of the National Cancer Institute, volume 90, 1998, pages 766-771].

Claim 33 claims the use of a Gleason score for analysis of the prognosis.

Claim 36 claims a nomogram for determining the risk of progression of prostate cancer after local therapy for prostate cancer or the risk of non-prostate confined cancer in a human prostate cancer patient comprising: at least one correlation, wherein the at least one correlation includes the correlation of the level or amount of at least one protein in a sample obtained from a human prostate cancer patient and the risk of

progression of the risk of non-prostate confined cancer in the patient, wherein the protein is selected from a group including TGF-beta1 and wherein the sample is obtained before or after therapy for clinically localized prostate cancer.

Ivanovic as applied to claims 28-31, 32, 34, 35, and 37-42 above does not show use of a Gleason score or a nomogram for data analysis.

Kattan et al. entitled, "A preoperative nomogram for disease recurrence following radical prostatectomy for prostate cancer." Column 2 on page 766 also shows use of a Gleason grade in analyzing prostate specific antigen (lines 29-30). Figure 2 on page 768 illustrates such a nomogram invoking Gleason scores.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to combine Ivanovic with Kattan to result in the instantly claimed invention because Kattan adds the ability to plot nomograms in the analysis of the prognosis and assessment of prostate cancer.

### ***Conclusion***

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

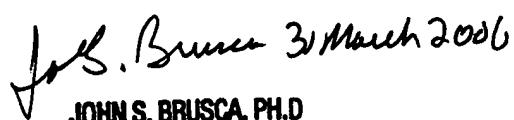
If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Ardin Marschel, Ph.D., Supervisory Patent Examiner, can be reached at (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

-RSN March 31, 2006

 3/31/2006

 3/31/2006

JOHN S. BRUSCA, PH.D  
PRIMARY EXAMINER